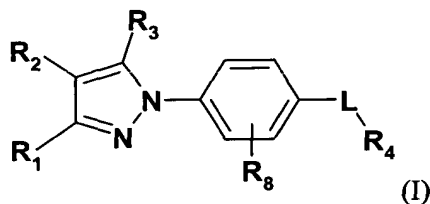


What is claimed is:

1. A method of treating a condition caused by endothelial dysfunction, said method comprising administering to a patient in need thereof a therapeutically effective amount of a compound of Formula I:



wherein:

- R₁** and **R₃** are the same or different and each is CF₃, halogen, CN, C₁₋₈ alkyl or branched alkyl, C₂₋₈ alkenyl or C₃₋₈ branched alkenyl, C₂₋₈ alkynyl or C₃₋₈ branched alkynyl, C₃₋₈ cycloalkyl optionally substituted with OH, CN or methoxy, C₁₋₈ alkyloxy, C₁₋₄ alkyloxyC₁₋₄ alkyl, C₁₋₈ alkylthio, C₁₋₄ alkylthioC₁₋₄alkyl, C₁₋₈ dialkylamino, C₁₋₄ dialkylaminoalkyl, CO₂**R₅** where **R₅** is C₁₋₄ alkyl or C₂₋₄ alkenyl optionally substituted with carbocyclyl or heterocyclyl, aryl or **R₁** and **R₃** are heterocyclyl connected to the pyrazole in any position that makes a stable bond optionally substituted with halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, CN, (CH₃)₂N, CO₂CH₃, alkyloxy, aryl, heterocyclyl or **R₅**;

R₂ is H, halogen or methyl;

L is -NHC(O)-, -NHC(O)O-, -NHC(O)C(O)-, -NHC(S)-, -NH-, -NHC(O)NH, NHC(S)NH, NHCH₂, -NHCH(**R₆**)-, where **R₆** is H, CN or C₁₋₃ alkyl,

R₄ is C₁₋₈ alkyl, C₁₋₈ alkyloxy, C₁₋₈ alkylthio, C₁₋₈ alkylamino, C₁₋₄ alkyloxyalkyl, C₁₋₄ alkylthioalkyl, C₁₋₄alkylaminoalkyl, C₁₋₄dialkylaminoalkyl, carbocyclyl or heterocyclyl each optionally substituted with one or more halogen, -CN, -NO₂, SO₂NH₂ alkylthio, alkylsulfinyl, alkylsulfonyl or **R₇** where **R₇** is phenyl, heterocyclyl, C₃₋₆ cycloalkyl, C₁₋₆

alkyl, C₂₋₆ alkenyl, C₁₋₆ alkyloxyalkyl, C₁₋₄ alkyloxy, C₁₋₅ alkylamino, C₁₋₆ alkylthioalkyl, C₁₋₆ alkylsulfinylalkyl or C₁₋₆ alkylsulfonylalkyl, each R₇ in turn is optionally substituted with halogen, OH, alkyloxy, CN, COO-lower alkyl, -CONH-lower alkyl, -CON(lower alkyl)₂, dialkylamino, phenyl or heterocyclcyl;

5

R₈ is H;

or the pharmaceutically acceptable salts thereof;

with the proviso that when R₃ is alkyl or CF₃ and R₄ is pyridyl, then the pyridyl is substituted except that the substituents on the pyridyl cannot be halogen; and with the proviso that the following compounds are excluded: *N*-[4-(5-ethyl-3-pyridin-3-yl-pyrazol-1-yl)-phenyl]-nicotinamide; *N*-[4-(5-Ethyl-3-pyridin-3-yl-pyrazol-1-yl)phenyl]-1-methylindole-2-carboxamide; 4-(3-Cyanopropoxy)-*N*-[4-(5-cyano-3-pyridin-3-yl-pyrazol-1-yl)phenyl]benzamide; and *N*-[4-(5-cyano-3-pyridin-3-yl-pyrazol-1-yl)phenyl]-4-(3-[1,3]dioxolan-2-yl-propoxy)benzamide.

15

2. The method according to claim 1 and wherein:

in formula (I):

20

R₁ is C₁₋₈ alkyl or branched alkyl, C₃₋₈ alkenyl or branched alkenyl, C₃₋₈ alkynyl or branched alkynyl, C₃₋₈ cycloalkyl, C₁₋₃ alkyloxyC₁₋₃ alkyl, C₁₋₅ alkyloxy, C₁₋₃ alkylthioC₁₋₃ alkyl, C₁₋₅ alkylthio, CF₃, heterocyclcyl selected from tetrahydrofuranyl, pyridyl, furanyl or thiazolyl or aryl optionally substituted with halogen, C₁₋₄ alkyl, CN, alkyloxy or (CH₃)₂N;

25

R₂ is H;

R₃ is halogen, methyl, ethyl, CF₃, CN, cyclopropyl, vinyl, SCH₃, methoxy, heterocyclcyl selected from tetrahydrofuranyl, pyridyl, furanyl or thiazolyl or aryl optionally substituted with halogen, C₁₋₄ alkyl, CN, methoxy or (CH₃)₂N;

30

L is -NHC(O)-, -NH-, -NHCH₂-, -NHC(O)NH, and

R₄ is C₁₋₆ alkyl, carbocyclyl or heterocyclyl selected from pyridyl, pyrimidinyl, pyrazinyl,
 5 pyridazinyl, morpholinyl, thiomorpholinyl, pyrrolyl, imidazolyl, pyrazolyl, thienyl, furyl,
 isoxazolyl, isothiazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, quinolinyl,
 isoquinolinyl, indolyl, benzimidazolyl, benzofuranyl, benzoxazolyl, benzisoxazolyl,
 benzpyrazolyl, benzothiofuranyl, benzothiazolyl, quinazolinyl and indazolyl, each
 optionally substituted with one or more halogen, -CN, alkylthio, alkylsulfinyl,
 10 alkylsulfonyl, -NO₂, SO₂NH₂ or **R₇** where **R₇** is C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆
 alkyloxyalkyl, C₁₋₄ alkyloxy, C₁₋₅ alkylamino, or C₁₋₆ alkylthioalkyl each optionally
 substituted with OH, CN, -COO-lower alkyl, -CONH-lower alkyl, -CON(lower alkyl)₂,
 dialkylamino, phenyl or heterocyclyl as hereinabove described in this paragraph.

15

3. The method according to claim 2 and wherein:

in the formula (I)

20 **R₁** is ethyl, isopropyl, *n*-propyl, *t*-butyl, cyclopentyl, CF₃, ethoxy, CH₃OCH₂-, 2- or 3-
 tetrahydrofuranyl, 2-, 3-, or 4-pyridyl, 2-furanyl, or 2-thiazolyl;

R₃ is CN, CF₃, Cl, methyl, ethyl, SCH₃, cyclopropyl, vinyl or 2-furanyl;

25 **L** is -NHC(O)-,
 and

R₄ is a phenyl or pyridyl each optionally substituted with one to three halogen, -CN,
 alkylthio, alkylsulfinyl, alkylsulfonyl or **R₇** where **R₇** is C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆
 30 alkyloxyC₁₋₆ alkyl, C₁₋₄ alkyloxy, C₁₋₅ alkylamino each optionally substituted with halogen,

OH, CN, COO-lower alkyl, -CONH-lower alkyl, -CON(lower alkyl)₂, dialkylamino, phenyl, morpholinyl or pyridyl.

5 4. The method according to claim 3 and wherein:

in the formula (I)

R₁ is isopropyl, CF₃, 3-pyridyl or 4-pyridyl;

10

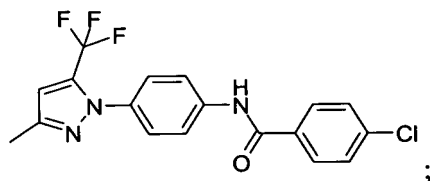
R₂ is H;

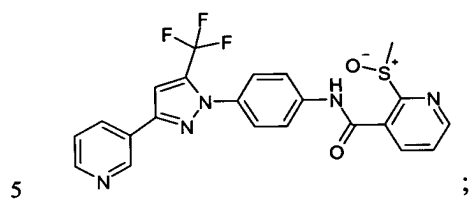
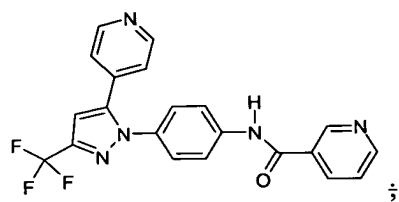
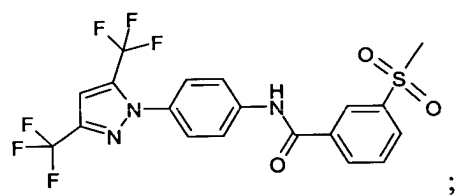
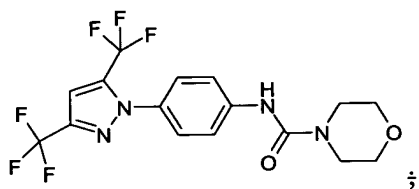
R₃ is CN, CF₃, Cl, methyl, SCH₃ or ethyl;

15 and

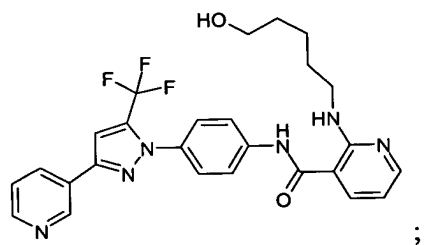
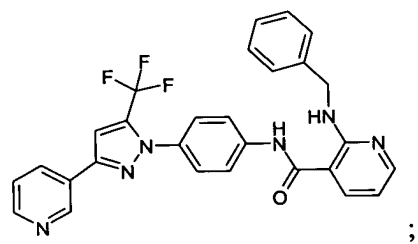
R₄ is a phenyl or pyridyl each optionally substituted with one to three groups selected from halogen, -CN, alkylthio, alkylsulfinyl, alkylsulfonyl or **R₇** where **R₇** is C₁₋₆ alkyl, C₁₋₄ alkyloxy, C₁₋₅ alkylamino each optionally substituted with OH, CN, COO-lower alkyl, -
20 CONH-lower alkyl, -CON(lower alkyl)₂, dialkylamino, phenyl, morpholinyl or pyridyl.

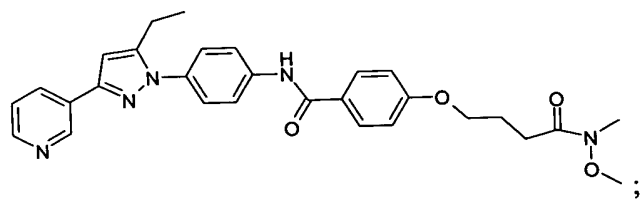
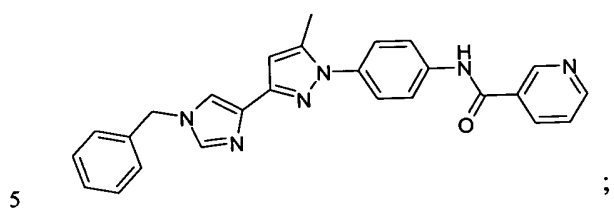
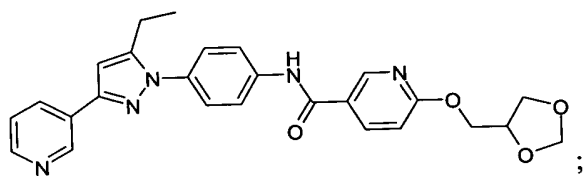
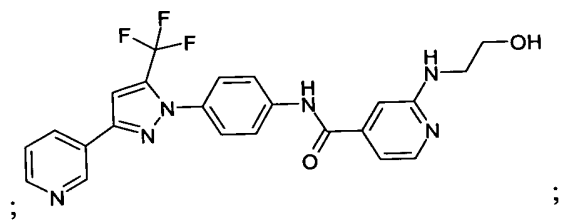
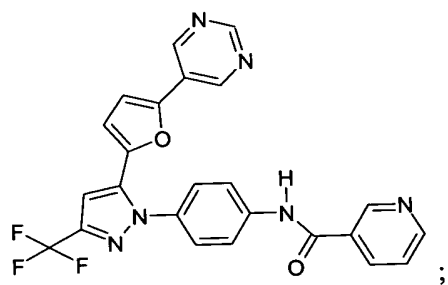
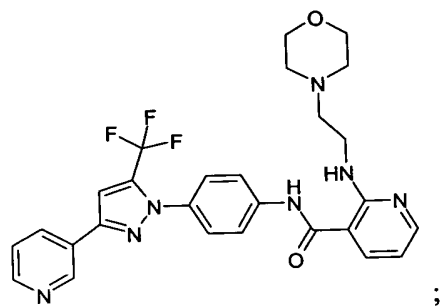
5. A method of treating a condition chosen from insulin resistance syndrome, hypertension, angina, ischemia, ischemic stroke, renal disease and Raynaud's disease, wherein said
25 condition is caused by endothelial dysfunction, said method comprising administering to a patient in need thereof a therapeutically effective amount of a compound chosen from :

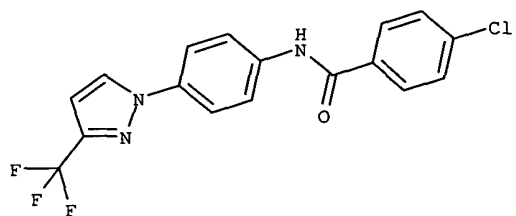




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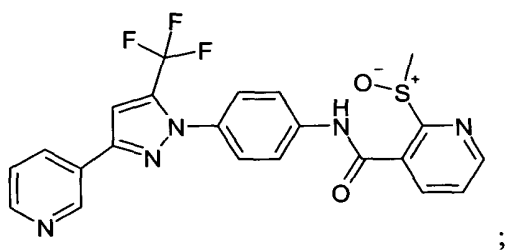




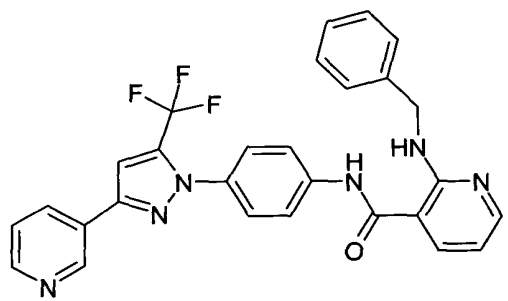
or the pharmaceutically acceptable salts thereof.

6. The method according to claim 5 wherein the compound is chosen from:

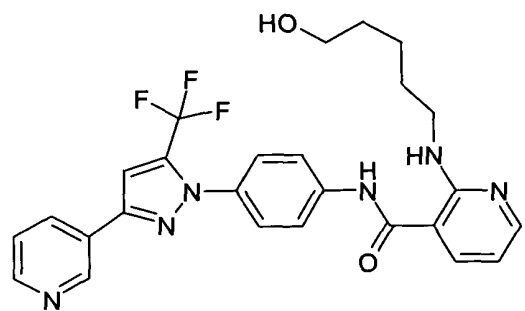
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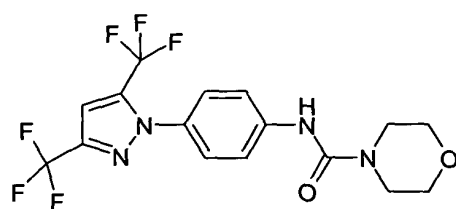
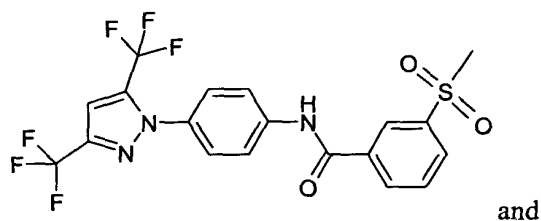
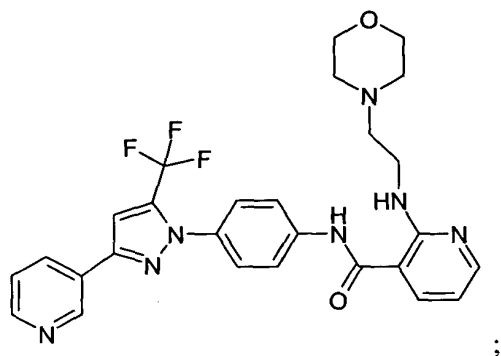
;



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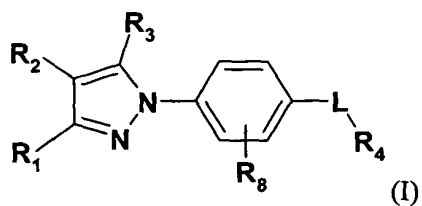
;



5

7. The method according to claims 1 or 5 wherein the condition is hypertension.

8. A method of increasing EETs concentration in a patient wherein said patient requires treatment of a condition caused by endothelial dysfunction, said method comprising administering to a patient in need thereof a therapeutically effective amount of a compound of Formula I:



wherein:

R₁ and **R₃** are the same or different and each is CF₃, halogen, CN, C₁₋₈ alkyl or branched alkyl, C₂₋₈ alkenyl or C₃₋₈ branched alkenyl, C₂₋₈ alkynyl or C₃₋₈ branched alkynyl, C₃₋₈ cycloalkyl optionally substituted with OH, CN or methoxy, C₁₋₈ alkyloxy, C₁₋₄ alkyloxyC₁₋₄ alkyl, C₁₋₈ alkylthio, C₁₋₄ alkylthioC₁₋₄alkyl, C₁₋₈ dialkylamino, C₁₋₄ dialkylaminoalkyl, CO₂**R₅** where **R₅** is C₁₋₄ alkyl or C₂₋₄ alkenyl optionally substituted with carbocyclyl or heterocyclyl, aryl or **R₁** and **R₃** are heterocyclyl connected to the pyrazole in any position that makes a stable bond optionally substituted with halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, CN, (CH₃)₂N, CO₂CH₃, alkyloxy, aryl, heterocyclyl or **R₅**;

R₂ is H, halogen or methyl;

L is -NHC(O)-, -NHC(O)O-, -NHC(O)C(O)-, -NHC(S)-, -NH-, -NHC(O)NH, NHC(S)NH, NHCH₂, -NHCH(**R₆**)-, where **R₆** is H, CN or C₁₋₃ alkyl,

R₄ is C₁₋₈ alkyl, C₁₋₈ alkyloxy, C₁₋₈ alkylthio, C₁₋₈ alkylamino, C₁₋₄ alkyloxyalkyl, C₁₋₄ alkylthioalkyl, C₁₋₄alkylaminoalkyl, C₁₋₄dialkylaminoalkyl, carbocyclyl or heterocyclyl each optionally substituted with one or more halogen, -CN, -NO₂, SO₂NH₂ alkylthio, alkylsulfinyl, alkylsulfonyl or **R₇** where **R₇** is phenyl, heterocyclyl, C₃₋₆ cycloalkyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkyloxyalkyl, C₁₋₄ alkyloxy, C₁₋₅ alkylamino, C₁₋₆ alkylthioalkyl, C₁₋₆ alkylsulfinylalkyl or C₁₋₆ alkylsulfonylalkyl, each **R₇** in turn is optionally substituted with halogen, OH, alkyloxy, CN, COO-lower alkyl, -CONH-lower alkyl, -CON(lower alkyl)₂, dialkylamino, phenyl or heterocyclyl;

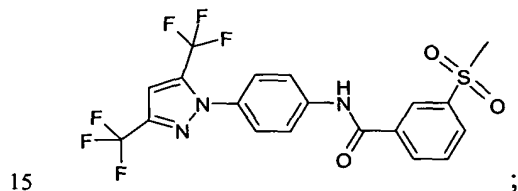
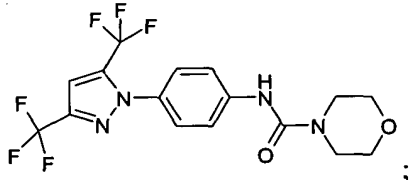
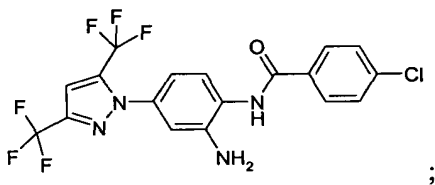
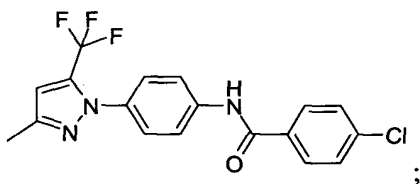
R₈ is H or NH₂;

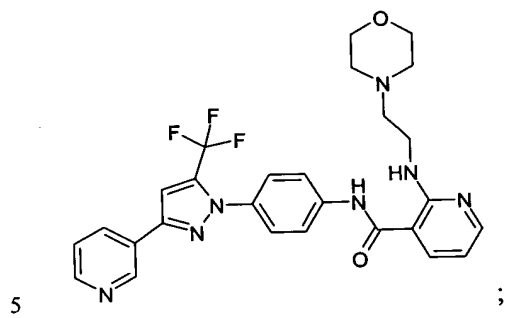
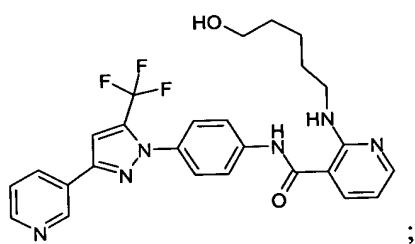
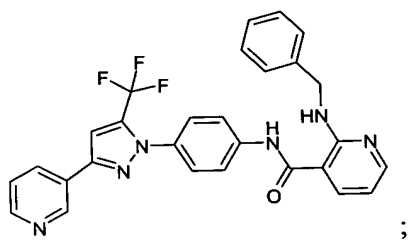
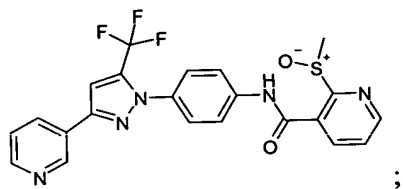
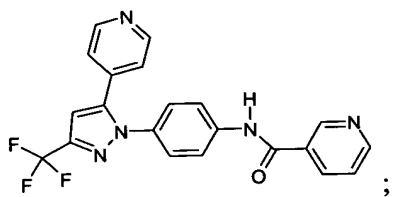
or the pharmaceutically acceptable salts thereof;

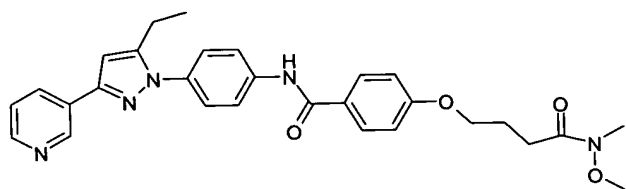
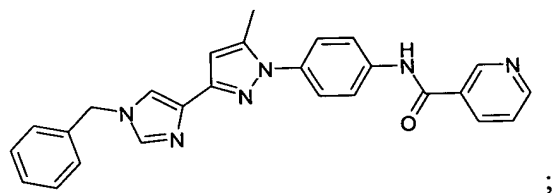
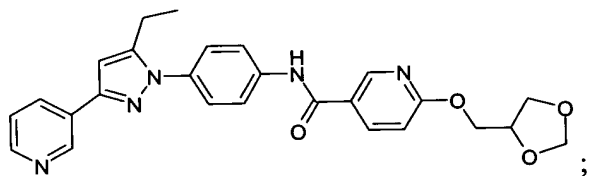
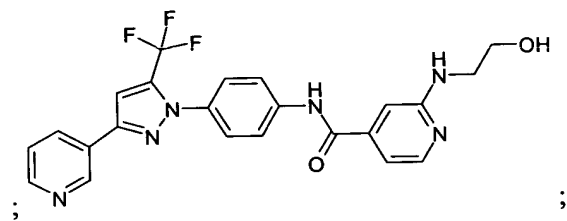
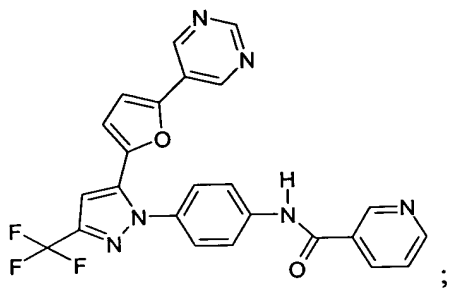
with the proviso that when **R₃** is alkyl or CF₃ and **R₄** is pyridyl, then the pyridyl is substituted except that the substituents on the pyridyl cannot be halogen;

and with the proviso that the following compounds are excluded: *N*-[4-(5-ethyl-3-pyridin-3-yl-pyrazol-1-yl)-phenyl]-nicotinamide; *N*-[4-(5-Ethyl-3-pyridin-3-yl-pyrazol-1-yl)phenyl]-1-methylindole-2-carboxamide; 4-(3-Cyanopropoxy)-*N*-[4-(5-cyano-3-pyridin-3-yl-pyrazol-1-yl)phenyl]benzamide; and *N*-[4-(5-cyano-3-pyridin-3-yl-pyrazol-1-yl)phenyl]-4-(3-[1,3]dioxolan-2-yl-propoxy)benzamide.

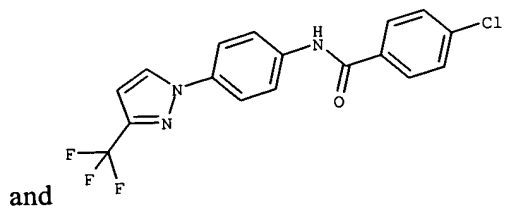
9. A method of increasing EETs concentration in a patient wherein said patient requires treatment of a condition caused by endothelial dysfunction, said method comprising administering to a patient in need thereof a therapeutically effective amount of a compound
10 chosen from:







5



and

or the pharmaceutically acceptable salts thereof.